REMARKS

Claims 4 to 8, and 24 to 39 are now in the case.

Claims 4, 8, 24, and 25 have been amended. Claims 30 to 39 are newly added, and claims 5 to 7 and 26 to 29 remain unchanged.

Reconsideration of this Application and entry of the foregoing amendments are requested. Claims 4, 8, 24, and 25 have been amended in view of the Office Action and to better define what the Applicants consider their invention, as fully supported by an enabling disclosure. Claims 30 to 39 have been added.

Additional support for the amendments to claims 4 and 24 regarding hybridization conditions can be found, for example, at page 23, lines 1 to 21. Claims 4 and 24 have also been amended to recite a functionality of the claimed Staufen sequences. Support for such biological functions of Staufen sequences may be found for example in figure 3 (RNA binding assay), figure 5, example 16, page 55 lines 17-21, page 56 lines 18 to 25, example 18, page 62 lines 3 to 8, example 10, page 50 lines 13 to 27, page 51 lines 1 to 6, and example 12, page 52 lines 8 to 10. Additionnal support for the tubulin binding activity of Staufen sequences can be found in example 11, page 51 lines 11 to 23, example 12, page 52 lines 12 to 19, example 16, page 57 lines 15 to 16 as well as in figure 5. Finally, additionnal support regarding Staufen's interaction with HIV genomic RNA can be found in example 18, page 62, lines 1 to 15, figure 8, figure 10, example 19, page 64, lines 16 to 19, page 65, lines 9 to 13, example 21, lines 1 to 5, page 68, lines 10 to 12 and lines 23 to 27. Support for the use of the term "95% identical" may be found for example in previously presented claims as well as in figure 1 (sequence comparison between human and murine Staufen proteins).

Claim 4 has also been amended to include a new subparagraph "(j)" which relates to a polynucleotide sequence which hybridizes under high stringency conditions to any of the polynucleotide sequences as set forth in SEQ ID NOs 1, 3,

5, 6 and 7; but does not hybridize to nucleotides 3073-3435 of SEQ ID NO:1, nucleotides 2784-3164 of SEQ ID NO:3, nucleotides 2709-3085 of SEQ ID NO:5, nucleotides 2914-3085 of SEQ ID NO:6 or nucleotides 2248-2770 of SEQ ID NO:7. Additionnal support concerning the use of functional fragments of Staufen sequences can be found in the description, for example at page 29, lines 14 to 27 and at page 30 lines 1 to 11.

New claims 32 and 36; 33 and 37; 34 and 38; and 35 and 39, are identical, except for their dependency to claims 5, 6, 7, and 8, respectively.

Applicants submits that no new matter has been entered by the foregoing amendment.

Applicants first note the Examiner's conclusion that the nucleic acid sequences of SEQ ID NO 1, 3, 5, 6 and 7 that encode a polypeptide disclosed in SEQ ID NO 2, 4, 8 and 10 are free of prior art of record. Secondly, Applicants have amended claims 4-8 to reflect the elected invention drawn to a human or mouse Staufen nucleic acid sequence as requested by the Examiner. Therefore, references to *C.elegans* nucleic acids have been withdrawn from these claims. Applicants reserve the right to prosecute the cancelled subject matter in further applications.

REJECTIONS UNDER 35 U.S.C. § 112 FIRST PARAGRAPH

The Examiner has rejected claims 4-8 and 24-29 under 35 U.S.C. § 112, first paragraph. The Examiner alleges that

> "the specification, **while being enabling for** (i) an isolated nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO 1, 3, 5, 6, and 7, (ii) an isolated nucleic acid encoding the amino acid sequence of SEQ ID NO 8, SEQ ID NO 10, SEQ ID NO2, SEQ ID NO 4, amino acid residues 1-577 and 2-577 of SEQ ID NO 2, amino acid residues 2-487 of SEQ ID NO 8, and amino acids 2-496 of SEQ ID NO 4 and (iii) a nucleic acid complementary to the full length nucleic acids of (i)-(ii), a recombinant vector comprising the isolated nucleic acid, a method of making a recombinant host cell comprising the isolated nucleic acid, a host comprising the nucleic acid, and a method of making a recombinant host cell comprising the isolated nucleic acid, does not provide enablement for nucleic acid encoding proteins that have at least

> **95% identity** to an isolated nucleic acid encoding amino acid of SEQ ID NO 8, SEQ ID NO 10, SEQ ID NO 2, SEQ ID NO 4, amino acid residues 1-577 and 2-577 of SEQ ID NO 2, amino acid residues 2-487 of SEQ ID NO 8 and amino acids 2-496 of SEQ ID NO 4." [Emphasis added]

The Examiner further alleges that the specification does not enable any person skilled in the art to which it pertains, to make and use the invention commensurate in scope with these claims. The Examiner reiterate his rejection of claims 4 and 24 for the reciting of a sequence 95% identical to recited sequences. The Examiner maintains his opinion that since the disclosure does not teach which 5% of the recited nucleotides could be substituted without altering the activity of the encoded protein, it is not enabling for such wording. The Examiner further notes that the specification does not teach how to use a nucleic acid that would encode a non-functional protein.

The applicants respectfully traverse this rejection as follows. Claims 4 and 24 have been amended to recite a functionality of the claimed Staufen sequences. The objection "95% identical" language is now found in a subparagraph in which it is recited that the "at least 95% identical" sequence encodes a Staufen polypeptide which retains a Staufen biological activity, namely its interaction with RNA, HIV genomic RNA or tubulin. Therefore, the claims are drawn specifically to functional Staufen proteins. Since the specification clearly teaches how to use functional Staufen proteins, and since the specification provides alignments of Staufen protein sequences, the Applicants submit that the amended claims are clearly enabled to a person of ordinary skill to which the present invention pertains. Applicants further stress that the field of structure-function relationship of proteins has literally exploded since the publication of Rudinger cited by the Examiner, which dates back to 1976. Indeed since then, many techniques, bioinformatic tools, crystallographic and RMN studies, mutagenesis of polynucleotides to specifically mutagenize the encoded proteins sequences...etc., are now very well known in the art. In fact, one could argue that in 1976, it was ancient times for the field of molecular biology and structure-function relationship of proteins, as compared to the date of filing of the instant invention (of note HIV was only identified in 1983). Presently, three mammalian genomes have been fully sequenced, and the methods

mentioned above are performed in undergraduates courses routinely. Thus, Applicants reiterate that in view of (1) the teachings of the mouse and human Staufen proteins in the disclosure; (2) the sequence-functions relationship found therein; and (3) the state of the art at the time of filing of the application, that a person of ordinary skill would without undue experimentation identify sequences that are 95% identical to the claimed sequences but yet retain at least one Staufen biological function.

The Examiner also maintains his objection regarding sequences that hybridize to sequences (a) to (h) of claim 4 or sequences of (a)-(f) of claim 24 under high stringency conditions. The Examiner states that some of the hybridizing sequences would be non-functional and that the specification does not teach how to use non-functional Staufen polypeptides. Furthermore, the Examiner notes that based on an artisan's interpretation, high stringency conditions may vary.

Claims 4 and 24 have been further amended to specifically recite highly stringent hybridization condition under which the claimed polynucleotide would hybridize. By specifying a particular set of condition, the variability objection has been rendered moot. Applicants stress that the terminology "highly stringent conditions", or the like, are very well known in the art and while a number of buffers and conditions can be used, this terminolgy is understood as being clearly defined by a person of ordinary skill. The claims further specify that the recited polynucleotide sequences encode a Staufen polypeptide which retains a Staufen biological function. Thus, it is respectfully submitted, that the objection for lack of enablement for non-functional Staufen has also been overcome.

In section 6, of the Official Action the Examiner notes that sequences at least 95% identical to recited polynucleotides encoding a Staufen polypeptide would also include nucleic acid molecules from organisms not disclosed in the specification. The Examiner argues that "the specification does not provide any disclosure as to what would have been the sequences structure of broad genus of sequences encompassed by the claimed invention." He further alleges that no other

relevant characteristics (i.e. other than the nucleotide sequences) enable to distinguish different members of the claimed genus and that several sequences may meet the sequence identity characteristic but may not be functional or have other characteristics.

As stated above, Claims 4 and 24 have been amended to include a functional limitation for the claimed sequences that are at least 95% identical to recited polypeptides sequences. Indeed the 95% identical sequences as recited as retaining at least one of Staufen's biological. Thus, Applicants submit that the claimed sequence contain an additional "relevant characteristic".

In view of the combination of 95% identity and functionality, only closely related proteins in sequence and function would meet both requirements (i.e. the sequence and function requirements). Furthermore, the description discloses how to use these functional Staufen proteins as examplified with two specific mammalian species (i.e. human and mouse). Moreover, the different interacting activities disclosed in the application enable to distinguish different members of the claimed genus. For example, binding to tubulin may be used to distinguish mammalian Staufen proteins from drosophila Staufen protein since the *Drosophila* polypeptide does not contain a tubulin binding domain and therefore does not bind to tubulin. The description disclose several *in vitro* assays (*in vitro* interaction with synthetic RNA, and tubulin or assessment of HIV viral infectivity) that may be used to assess Staufen's biological activity. A person of ordinary skill in the art can therefore use these assays, or other assays known in the art, to determine whether sequences having 95% identity with the claimed sequences display a Staufen biological activity. The Applicants believe that the description sufficiently disclose how to identify and use such 95% identical Staufen and therefore respectfully request that the rejection be withdrawn.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraws his rejection of claims 4-8 and 24-29 under 35 U.S.C. § 112, first paragraph.

REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claim 24 have been rejected under 35 U.S.C. § 112, second paragraph as being indefinite. The Examiner alleges that the use of the terminology *"polynucleotide sequence being identical to a sequence"* in the preamble, renders the claim indefinite. The Applicants respectfully submits that in view of the cancellation of this terminology from the preamble, this rejection has been overcome.

In view of the above and foregoing, it is respectfully requested that the Examiner withdraws his rejection of claims 24 under 35 U.S.C. § 112, second paragraph.

REJECTION UNDER 35 U.S.C. § 102

Claims 4 and 24 have been rejected as being anticipated by Marra *et al.* (Accession No. AA122533, Database EST, 2-17-97) and Banfi *et al.* (Accession no G30939, Database GenEmbl, 9-29-98; Nature genetics 13:167-174, 1996) under 35 U.S.C. § 102(b) and (a), respectively.

The Examiner alleges that Marra *et al.* "teach a 522 bp nucleic acid sequence that has 99.8% best local sequence similarity with nt 2248-2770 of SEQ ID NO 7" of murine Staufen. Marra sequences are further alleged to hybridize to SEQ ID NO 7 under stringent conditions. Applicants traverse the rejection over Marra as follows.

The portion of SEQ ID NO 7 with which the Marra sequence possesses similarity is a portion of the 3' UTR region. Hence it hybridizes to the non-coding region of Staufen polynucleotide. The Applicants respectfully submit, that in view of the recitation "encoding", "encoding a Staufen polypeptide", "which encodes a Staufen polypeptide sequence", and "fully complementary" that claims 4 and 24 are free of prior art since the Marra sequence cannot encode a functional Staufen polypeptide, because it does not encode any polypeptide.

The Examiner also alleges that Banfi *et al.* discloses a 385 bp sequence which has 99.2% sequence similarity with nt 2705-3089 of SEQ ID NO 1, 3069-3453 of SEQ ID NO 1 and 2911-3295 of SEQ ID NO 6 and therefore would hybridize to SEQ ID NO 1 and 6 under stringent conditions.

The Applicants respectfully believe that the Examiner ment nt 3073-3435 of SEQ ID NO1, 2784-3164 of SEQ ID NO3, 2709-3085 of SEQ ID NO 5 and 2914-3085 of SEQ ID NO 6. According to Banfi *et al.* (and to the Examiner), the 385 bp nucleic acid sequence would indeed hybridize under stringent condition to SEQ ID NO 1, 3, 5 and 6. However, the Banfi sequence again only possesses similarity to the 3'UTR region of the human Staufen sequence. Since claims 4 and 24 are directed to polynucleotide sequences which encode functional Staufen polypeptides, it should be clear that both claims are free of Banfi *et al.* which teaches non-coding sequences of Staufen.

Applicants wish to stress that for the most part, claim 4 is restricted to polynucleotide sequences encoding specific amino acid sequences (SEQ ID NO 2, 4, and 8) and hence do not include the 3'UTR region of mouse or human Staufen. Therefore, such sequneces in claim 4 are indeed be free of sequences taught by either of Banfi or Marra.

Claim 4 also includes in a new subparagraph (4-j) which relates to a polynucleotide sequence which hybridizes under high stringency conditions to any of the polynucleotide sequences as set forth in SEQ ID NOs 1, 3, 5,6 and 7; but does not hybridize to nucleotides 3073-3435 of SEQ ID NO:1, nucleotides 2784-3164 of SEQ ID NO:3, nucleotides 2709-3085 of SEQ ID NO:5, nucleotides 2914-3085 of SEQ ID NO:6 or nucleotides 2248-2770 of SEQ ID NO:7. These hybridizing sequences exclude all of the Marra or Banfi sequences and are therefore free of prior art.

Thus in view of the above and foregoing, Applicants respectfully request that the 35 USC § 102 rejections be withdrawn, since the claimed sequences are free of Marra or Banfi.

CONCLUSIONS

The rejections of the claims are believed to have been overcome by the present remarks and the introduction of new claims. From the foregoing, Applicants respectfully submit that a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

Authorization is hereby given to charge deposit account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,

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